# INTERNATIONAL HEALTH NEWS

*William R. Ware, PhD - Editor*

**NUMBER 246** **APRIL 2014** **23rd YEAR**

*The armament mainstream medicine takes into battle against disease prevention and treatment is primarily drug-based, although there are also medical devices such as pacemakers and implants such as artificial joints and the hardware used in back surgery. Thus it is of interest to look at the top drugs bringing in the most revenue to their manufacturers. Here is the list for the US published by the industry for 2012 (Pharmacy Times, July 17, 2013).*

1. *Nexium - Proton pump inhibitor for acid reflux ("purple pill" as seen on TV)*
2. *Abilify - Antidepressant*
3. *Crestor - Cholesterol lowering statin*
4. *Advair - Asthma*
5. *Cymbalta - Antidepressant*
6. *Humirsa - Rheumatoid arthritis*
7. *Enbrel - Rheumatoid arthritis*
8. *Remicade - Psoriasis*
9. *Copaxone - Multiple Sclerosis*
10. *Neulasta - Adjuvant for chemotherapy*

*This is an interesting list for the following reasons. Proton pump inhibitors are controversial since they alter the natural stomach acidity involved in primary digestion and have other serious side effects. Some integrative physicians cure acid reflux problems by increasing, not decreasing stomach acidy. For depression other than very severe, antidepressants have been shown to be no better than a placebo. For primary and secondary prevention of cardiovascular events, statins offer no benefit to between 97 and 99% of those who take them. Asthma drugs are not curative, but do treat a symptom which if untreated can be deadly. Drugs for rheumatoid arthritis offer mainly pain relief. A comparable global list omits Copaxone and Neulasta and adds Lantus, a diabetic drug and MabThera for rheumatoid arthritis. Thus globally, the same picture emerges.*

*If instead of ranking individual drugs, one ranks by the disorder, indication or complaint, globally, the top 10 therapeutic classes by sales (total about 290 billion US$) are as follows (ACS Chem Neurosci. 2013. 4, 905-907).*

1. *Oncology*
2. *Pain*
3. *Antihypertensive*
4. *Anti-diabetic*
5. *Mental health, e.g. antidepressants, antipsychotics, stimulants (AHHD)*
6. *Respiratory*
7. *Antibacterial, e.g. antibiotics*
8. *Elevated cholesterol*
9. *Autoimmune disorders*
10. *Anti-acids or anti-ulcerants*

*The similarity of the two lists is interesting. The order changes because there is a significant variation in the number and popularity drugs for each indication. Oncology uses a wide variety of pricy chemicals. The appearance of anti-diabetic drugs high on the second list is also an indication of the large number of agents in use. However, as has been discussed in IHN, the control of blood sugar they achieve has very limited impact on the long-term outcomes for those with type 2 diabetes.*

*The picture that emerges is consistent with the editorial in the March IHN, since these lists reflect mostly treatment rather than prevention. Treatment is mainly for symptoms, mostly not curative, and successful prevention is restricted to a very small percentage of those treated. Mainstream medicine correctly tells us that prevention is better than treatment, but Big Pharma has failed to provide practitioners with the only tool commonly used. And it is pills that the public want. Advice on lifestyle and diet may be provided, but appears to have little impact.*

*Finally, if you need to restock your supplements, please remember that by ordering through the on-line vitamin store you will be helping to maintain the web site and publication of IHN. You can find the store at http://www.yourhealthbase.com/vitamins.htm.*

*Wishing you and your family good health,*

***William R. Ware, PhD, Editor***

**Highlights**



# TOXINS AND THE DEVELOPING BRAIN

***Better things or better living through chemistry.*** **DuPont, 1935**

***THE BIG PICTURE***

Disabilities implicating the brain appear to be steadily increasing and the problem is seen at all ages. Of particular concern are the neurodevelopmental disabilities seen in children including autism, attention deficit-hyperactivity disorder, dyslexia, cognitive problems and learning disabilities. The current prevalence of some of these disorders suggests a disaster is unfolding before us with profoundly serious ramifications for the victims, parents, educators and society in general. Prevalences of 1 in 20 or less, as seen in some disorders should be regarded as a crisis demanding a herculean effort to positively identify the real causes and improve therapy. Of particular concern are disorders which imply a permanently damaged brain. Treating symptoms or managing marginal improvements of neurobehavioral developmental problems while waiting for wonderfully effective and safe drugs is simply not good enough.

In an article just published online in the journal *Lancet-Neurology*, Philippe Grandjean (University of Southern Denmark and Harvard) and Philip Landrigan (Harvard) provide an in-depth review and analysis of neurobehavioral development effects which can be associated with the action of environmental toxins.[1] This paper is a sequel to a 2006 study where the authors identified 5 industrial chemicals that could be reliably identified as developmental neurotoxins. They also noted 201 chemicals that had been reported to cause nervous system injury in adults, mostly through occupational exposure. In that paper they also commented that there were more than 1000 chemicals that had been reported to be neurotoxic in animals.

The authors also point out that the root causes of the present global pandemic of neurodevelopment disorders are only partly understood. While recognizing the potential role of genetic factors, they take the position that these cannot explain the recent increased prevalence and none of the potentially important genes appear to be responsible for more than a small percentage of cases. The conclusion—environmental exposures are implicated in causation, perhaps with some interaction between toxins and genes (epigenetic effects), and that these exposures account for 60-70% of all cases.

It is generally recognized that the developing human brain is acutely vulnerable to toxic chemical exposure and that there are many windows in time where specific vulnerability exists, starting in utero and extending to infancy and childhood. During these periods of development, chemicals can cause permanent brain injury at levels of exposure so low that they would have little or perhaps no impact on adults. All one needs to do is reflect on the immense complexity of the programmed processes starting with the fertilized egg, i.e. one cell and ending up with a newborn having about a thousand billion cells, and if all has gone well, everything of the normal size and shape and all of the vast number of systems and biochemical processes working normally. It requires little imagination to comprehend how a toxin can adversely alter or stop some biochemical or microbiological process with the impact in some cases minor, but in some cases a disaster potentially permanent and even fatal to the fetus.

A major problem is that the clinical manifestations of the toxin induced disorder may be significantly delayed, even by years, and subclinical symptoms easily ignored or absent. Prenatal and early postnatal exposure to arsenic, for example from drinking water, is associated with cognitive effects that only become apparent at school age. The authors cite a comment by the former director of the US National Institutes of Environmental Health Sciences that if thalidomide had caused a ten point decrease in IQ rather than horrific birth defects of limbs, it would probably still be on the market. Incidentally, there was a remarkably small time window during gestation where this toxic effect occurred, which emphasizes the observation regarding the complexity of the toxic action.

***THE DEVELOPING BRAIN IS UNIQUELY VULNERABLE***

Grandjean and Landrigan cite the following:

- Contrary to common belief, the fetus is not well protected. More than 200 chemicals foreign to humans have been found in umbilical cord blood.
- Infants also acquire toxins through breast milk.
- During gestation and early life, the blood-brain barrier provides only partial protection from chemicals entering the central nervous system.
- Stem cells are particularly sensitive to toxic injury.
- Early–life interactions between toxins and genes are known to affect subsequent gene expression in the brain.
- There is no safe level of exposure to lead, and developmental delays at school age are probably permanent.
- Developmental neurotoxicity to mercury (organic) occurs at levels lower than concentration affecting adult brain function.
- Maternal consumption of alcohol during pregnancy has been linked to a number of neurobehavioral problems in offspring. The point is that these occur even at very low levels of consumption. Documented adverse effects include reduced IQ, impaired executive function and social judgement, delinquent behavior, seizures, and sensory problems. Alcohol is probably one of the most easily avoided toxins during pregnancy.

***RECENTLY RECOGNIZED AND OTHER NEURODEVELOPMENTAL TOXINS***.
Maternal or fetal exposure to toxins can be measured, albeit with limitations, and this provides the opportunity for highly informative follow-up studies. Information includes the timing of and degree of exposure during the prenatal period. Grandjean and Landrigan provide a number of examples with documentation.

- Manganese from drinking water has been associated with poor school achievement, hyperactivity, diminished intellectual function and reduced motor skills.
- A meta-analysis of 27 studies of fluorine in drinking water revealed reduced IQ of about 7 points.
- Maternal solvent exposure in the workplace has been related to deficits in behavior assessment at age 2. Job exposure was common in nursing, other hospital jobs, as well as jobs as a chemist, cleaner, hairdresser and beautician. The solvent perchloroethylene in drinking water was related to neurological deficits.
- Prenatal exposure to organophosphate pesticides has been found to correlate with small head circumference at birth and neurological effects that persisted to at least 7 years.
- Herbicides and fungicides are also implicated. Propoxur, a carbamate pesticide, and permethrin have recently been linked to impaired neurodevelopment in children.
- Flame retardants, a common household toxin found in furniture, mattresses, insulation and emitted from electronic equipment, have been shown associated with neurodevelopment deficits in children with prenatal exposure.
- Prenatal exposure to phthalates has been linked to both behavioural problems associated with reduced attention span and impaired social interactions and neurodevelopmental deficits.
- Prenatal exposure to bisphenol A has been found to be associated with behavioural abnormalities in children apparent by age 3.
- Air pollutants such as carbon monoxide and aromatic hydrocarbons are implicated in lower IQs and cognitive impairment in children.

In the seven years since the 2006 paper, the number of authenticated developmental neurotoxins has doubled from six to twelve. The fact that brain development is a sequential process means that prenatal neurotoxic damage may not become apparent until school age or beyond. Recognition of developmental neurotoxicity and its association with toxins depends on data collected from the mother during gestation and data from the child's postnatal neurobehavioral development. This is in contrast to adult data generally associated with prompt evidence due to workplace exposure or suicide attempts.

***THE BOTTOM LINE***
Grandjean and Landigan cite a recent study which illustrates the magnitude of the problem being discussed. The issue was damage to the brain that lasts a lifetime and was measured by lost IQ points. The magnitude of the losses due to lead, pesticides and other neurotoxins was of the same magnitude as that associated with preterm birth, brain injury due to trauma, brain tumors and congenital heart disease. Children are being deprived of a normal life and the opportunity to reach their natural potential by poisons to which they and their mothers are exposed, generally unknowingly, and yet in many cases, the toxic chemicals are declared safe not only by the producers but by official government agencies. As discussed in IHN last month, only minute amounts are necessary for there to be many atoms or molecules of toxin available to every cell in the newborn child. Furthermore, maternal toxic burden is impossible to accurately assess. Huge and powerful commercial interest are involved in maintaining the notion that there is no problem

The paper by Grandjean and Landigan was instantly met with well-publicized criticism and dismissal by the major association that represents chemical company interests. And indeed, the industry holds most of the cards. New chemicals are assumed safe until proven otherwise and some of the classic, now banned chemicals produced great harm before finally being

removed from the market. Critics describe the problem as industrial epidemics. It also seems quite certain that progress in reducing the toxic environment so carelessly created will be frustratingly slow.

So, what to do? Wait for stricter controls? Wait for more studies? Both are clearly needed but will not solve the immediate problem of body loads of toxins already present and the continual exposure which is mostly hidden. The industries which would be hurt by stricter controls and active surveillance of toxins encountered every day have over the years developed techniques of an almost unimaginable variety to combat any threat. Their ingenuity in this area is comparable to their ingenuity in developing new products. These methods are proven very successful in delaying action, discounting unfavourable research, discrediting critics, and controlling regulatory decisions. See for example Chapter 9, titled *Inconvenient Truths*, in Philippe Grandjean's recent book *Only One Chance.*[2] Thus it is not realistic to wait. A whole world may have been put at risk, this continues and change will probably be slow.

An answer to the threat posed by neurotoxins to the developing brain, both prenatal and in childhood, was partly provided in the last issue of IHN. Toxins must be avoided as best one can – not a simple matter. However, detoxification is the only comprehensive answer. Before conception, intentional interventional detoxification may be very important. This involves oral chelators and stimulants of innate detoxification obtained from food and supplements and the frequent induction of significant sweating. Some aspects such as avoidance are obviously appropriate for children. However, flame retardants which appear to be neurotoxins but are very difficult to avoid since they are frequently mandated for mattresses, carpets, insulation in newer homes, etc. present a serious problem. Detoxification of young children is something that must be left to experts, of which there are few who do this as part of a pediatrics practice and few who recognize its importance.

**N.B. It is important to realize that the risks during pregnancy of using supplements and oral chelators, or even saunas which assist in detoxification are unknown.**

## ENVIRONMENTAL FACTORS AFFECT INCIDENCE OF AUTISM AND INTELLECTUAL DISABILITY

An important study has just appeared which directly relates autism and intellectual disability to environmental toxins.[3] The investigators used an insurance database of 100 million patients and found clustering in counties across the US. They then used male congenital malformations as a surrogate for parental exposures to environmental insults such as from lead, sex hormone mimics, pesticides, and plasticizers. After adjusting for gender, ethnic and socioeconomic and geopolitical factors, they found that in the cluster counties, autism rates were strongly correlated with rates of male congenital malformations of the reproductive system. Accumulating evidence was cited (13 references) suggesting that the rate of these birth malformations could serve as an indicator of average parental exposure to toxins within a geographical unit. The results were shocking. An increase in the incidence of autism of 238% was found for every percent increase in the incidence of malformations in the same population. In addition, comorbidity analysis showed that male children with autism are over 5 times more likely to have congenital reproductive malformations than unaffected males, a result that had high statistical significance. Furthermore, congenital malformations in males of organs other than reproductive system were also correlated with a 32% increase in autism and a 43% increase in intellectual disability, although for intellectual disability, male reproductive deformities were only weakly associated. When the congenital birth defect risk was linked to parental occupation, there was a statistical significant increase in birth defects associated with maternal occupations as janitors, maids, and landscapers compared with other occupations.

The authors conclude that (1) autism and intellectual disability display strong clustering across US counties; (2) counties with high autism rates also appear to have high intellectual disability rates; and (3) the geographical variation appears to be driven by environmental factors and to a lesser extent by economic factors. The environmental factors are unmeasured developmental risk factors, including toxins. In other words, a toxic environment leading to a maternal toxic load which manifests itself in male reproductive birth defects and other birth defects was a surrogate indicator of toxic load, and this load was also high enough to strongly influence the incidence of autism. While obviously not conclusive proof, these results are highly suggestive of cause and effect. This study is a very important addition to the sparse set of studies involving humans in this context.

## PESTICIDE TOXICITY STUDIES DONE ON THE WRONG PRODUCT

In the March issue of IHN, problems were described that the French group lead by G. E. Seralini encountered after the publication of their study on tumors in mice produced by GM corn. It appeared that the paper was withdrawn by one of the editors without real justification. This group has just published a paper that will also annoy the pesticide-herbicide industry. Naturally, they submitted it to a different journal from the one that withdrew their mouse tumor study, in this case *Biomed Research International* which unfortunately is not covered by PubMed.[4]

The new study reveals a dirty little secret. The formulations of pesticides into the liquid preparations ready for application (generally with dilution) contain not only one ingredient considered the active agent for the desired toxicity, but a number of undeclared toxins which, as Seralini and coworkers found, are in some preparations vastly more toxic than the main ingredient. The point is that the toxicity studies used to establish “safe” human exposure do not test all ingredients, but examine only the main one and thus grossly underestimate the human toxic potential of the product used in the field. It is bad enough that the animal toxicity studies generally last only 90 days, the industry standard, which is not long enough to detect most of the important adverse effects, or that the intrinsic difference between animals such as mice and humans in this context is that animals have detoxification mechanisms that differ significantly from humans. Thus setting safe limits is a fantasy, even under the best of circumstances.

The study looked at three major herbicides, three insecticides and three fungicides. Each pesticide had one declared active ingredient and several so-called inert components. The investigators examined the cell toxicity from the percent survival as they increased the concentrations of either the active ingredient alone or the preparation as sold to farmers. Three different human cell types were used in these cell culture experiments. They found that the commercial preparations at agricultural dilution or less had up to 1000 times greater cell toxicity than the declared active ingredients.

While it is commonly believed that Roundup is among the safest pesticides, they found that it was by far the most toxic among the herbicides and insecticides examined when the commercial formulation was compared the active ingredient glyphosate. Roundup is one of the principal herbicides used in huge quantities worldwide and Roundup resistance is an integral aspect of some genetically modified crops.

# ACUTE KIDNEY INJURY, A SERIOUS ADVERSE EFFECT OF CORONARY CATHETERIZATION

Coronary catheterization, also known as balloon angioplasty but more properly called percutaneous coronary intervention (PCI), is a common procedure with over 600,000 procedures done annually in the US and about 60,000 in Canada. The procedure is mostly in response to angina or evidence of a heart attack. A catheter is inserted into a blood vessel in the groin or arm and guided by x-ray fluoroscopy as it is threaded through blood vessels to the heart, at which point a contrast medium is released. After a narrowing judged significant is located, the catheter is used to implant a metal stent using balloon inflation. In some hospitals, a protocol is in place to accelerate triage and speed patients viewed as a PCI candidate off to the so-called cath lab. Cath labs represent an excellent source of hospital income and one hears of cases of abuse.

Patients should expect a risk/benefit analysis prior to the procedure. Risks associated with the procedure include allergic reaction to the drug in the drug-releasing stent or a component of the contrast medium, a blood clot, damage to a heart valve or blood vessel, heart attack, acute kidney injury which can lead to kidney failure and dialysis, irregular heartbeats and stroke. The benefits include greatly improved coronary blood flow and avoiding the immediate need for coronary artery bypass surgery (CABG). This is a mechanical fix, not a cure for the cause and the fix may eventually fail. The risk/benefit analysis is complex and the benefits must also be weighed against aggressive non-invasive medical therapy or the alternative, CABG. It is not clear that patients who reach the cath lab via the intervention express route receive sufficient information and evaluation to make an informed consent. The atmosphere maybe supercharged with urgency and the patient may believe that the “life-saving” intervention is desperately needed. In some cases this is true.

If one examines the risk assessment discussions from professional medical organizations as seen on the internet, the risk of acute kidney injury is not emphasized. However, paper just published in *JACC: Cardiovascular Interventions*, contains results suggesting the risk is high, serious, and life threatening.[5] Furthermore, a thorough assessment with laboratory data is needed regarding kidney function which may not be available on short notice.

The study in question examined almost 1 million consecutive patients who underwent PCIs at 1253 sites participating in a national registry. The study covered the period from June 2009 to June 2011 and focused on the occurrence of acute kidney injury and in-hospital heart attacks and death following PCI. Acute kidney injury (AKI) was ascertained by comparing pre-procedure serum creatinine levels with post-procedure peak change. Pre-procedure kidney function was determined from serum creatinine levels used to calculate the glomerular filtration rate, a standard measure of kidney function (GFR on clinical lab reports).

It was found that AKI developed in 7.1% (70,000) of all the patients of whom 0.3% (3000) also required dialysis. The mortality rates for those with no PCI-related AKI, AKI or AKI requiring dialysis were 0.5%, 9.7%, and 34.3%. For heart attack, the numbers were 2.1%, 3.8% and 7.9% respectively. Thus the occurrence of PCI-related AKI strongly increased the risk of in-hospital death or heart attack. After adjusting for differences in patient characteristics at baseline, AKI was associated with significantly increased odds of mortality (268%) and heart attack (66%). For patients requiring dialysis the numbers were much larger, 356% and 170%. These results were all statistically significant. It was also reported that on stratification by the AKI stages, all stages were independently associated with heart attack and death. AKI also significantly increases the risk of bleeding. No stratification was made for the motivation for the PIC which ranged from elective diagnosis to response to an acute event.

The authors' comments imply that strategies to minimize the risk of AKI in patients undergoing PCI are needed to improve the safety and outcomes of this procedure. The iodinated contrast material used had been hypothesized to cause AKI, acting through direct toxicity and is the third leading causes of AKI in hospitalized patients, according to the authors. They suggest an attempt should be made to minimize the contrast dose. However, they do not mention the importance of kidney toxicity and the patient kidney function status in assessing the risk vs. benefit of PCI in determining the advisability of PCI.

If PCIs are being contemplated on patients where the procedure is inappropriate or uncertain, then the risk/benefit analysis may shift to too much risk just from AKI. This appears to be a problem based on a study using the same database and examining the question of appropriateness for the period July 2009 to September 2010, which involved examining the clinical data for 500,000 PCIs.[6] For acute indications, 98.6% of the procedures were considered appropriate. However, for non-acute presentations which characterized 29% of the patients having PCIs, half were found to be inappropriate (35% uncertain, 11.6% clearly not appropriate). It can be argued that this is the group where detailed assessment of the risk presented by kidney function should be factored into the risk/benefit equation. However, in general for those inappropriately treated, on must wonder if any meaningful risk/benefit analysis was done at all.

Another unresolved issue involves the three options, PCI, CABG or simply non-invasive aggressive medical therapy. This is a complex issue because of the large variety of presentations, comorbidities, age and endpoints. For example, the COURAGE trial found no mortality difference between aggressive medical therapy and PCI with bare metal stents added to aggressive medical therapy. The trial did show fewer subsequent revascularization procedures.

# NEWS BRIEFS

### A HEART INTERVENTION FACTORY (CATH LAB) EXPOSED BY BLOOMBERG NEWS REPORTING

On March 6, 2014, *Bloomberg News* ran a story on bizarre events found to be occurring at a famous New York City hospital. On Sunday mornings, patients were showing up at the ER claiming they had acute symptoms of heart disease. However, it turns out that they actually had appointments for PCI in the cath lab and had been coached as to the story they provided to the ER doctors. It also turns out that private insurers and Medicaid will pay for procedures done as a result of an ER visit that would not be covered otherwise. The Bloomberg investigative reporters were able to ascertain that this cath lab did over 4700 stent-related procedures in 2012 and that a typical charge was $20,000. The hospital also has maintained a "commanding lead" over other New York hospitals by doing 1500 more catheter-based treatments than any other, according to an internal report.

The point of bringing up this story is the above piece on the risks of acute kidney injury associated with PCI. The Bloomberg report, which readers are encouraged to download and examine, suggests overtreatment which would be putting patients at unnecessary risk of serious side effects. Cynics would merely say, what else is new?

In this context, there have been reports over a number of years of patients being bullied with regard to agreeing to invasive procedures after a heart attack, even though they are stabilized and want to go home. Doctor after doctor, nurses and even psychiatrists parade to the bedside in the ER making the case that it is either the intervention or almost certain sudden death. Patient refusal simply intensifies the pressure. Pressure is also put on the family. Somewhat of a hard sell circus. These accounts frequently are published in

newsletters written by prominent physicians, even cardiologists. Cynics would say that this high pressure sales job is being driven by the high profit margins of the cath lab.

## TESTOSTERONE THERAPY AND RISK OF CARDIOVASCULAR EVENTS

Testosterone therapy has made it to prime time with ads on the US main network nightly news programs. The underarm gel advertized is available only by prescription in the US. Advertizing campaigns of the magnitude we are seeing suggests robust sales and thus it is of interest to examine recent studies which suggest that testosterone therapy (TT) increases the risk of cardiovascular events, and in particular heart attacks.

A meta-analysis of 27 trials lasting 12 or more weeks and including 2994 older men recently appeared in the journal *BMC Medicine*.[7] When all studies were included, a 54% relative risk increase in cardiovascular-related events was found with an absolute risk increase of 1.5% based on treated and placebo events. However, when the investigators examined industry supported studies (13) vs. non-industry supported studies (14), for the former there was no significant increase in risk whereas for the latter, the relative risk in the treatment group was twice that in the placebo group with absolute risk increase of 5.5%. Most of the studies included were characterized by low numbers of events and thus insignificant results, but the one study with the largest number found a statistically significant 6 fold increase in risk.

A study just published in *PLOS ONE* looked at non-fatal heart attacks in 55,593 men following an initial prescription for testosterone.[8] The incidence rate of MI in the 90 days following the initial prescription was compared to the rate in the years prior to the initial prescription. Among men 65 years and older, a two-fold increase in the risk of MI in the 90 days after filling the TT prescription was observed, and the risk declined to baseline between 91 and 180 days. Among younger men with a history of heart disease a two- to three-fold increase in MI was found in 90 days with no excess risk in men without such a history. Among older men, the increased risk of MI was independent of cardiovascular history, but the analysis involved a small number of cases. This study had more MI cases than all 27 studies in the meta-analysis discussed above.

While much larger studies are needed, the above results suggest caution, especially when the non-industry supported studies yielded an absolute risk increase of 5.5%, It is worth noting that when industry supported studies are compared with non-industry ones, the frequent result is a large discrepancy such as described above. Most guidelines which essentially determine medical practice are based on industry supported clinical studies. No alternative support is available. The cost is prohibitive. Insight into the magnitude of the problem can be acquired by reading Ben Goldacre's recent book *Bad Pharma.*

## PREVENTING STROKE AMONG THE ELDERLY

A perspective just published in the BMJ journal *Evidence Based Medicine* nicely summarizes the merits of anti-hypertensive or lipid-lowering therapy in the context of stroke and cardiovascular mortality.[9] Statins and anti-hypertensive medications are widely used in patients over 80. In the US, 75% of the elderly are on statins for primary prevention. The author challenges this "orthodoxy" with the following points.

- Data from the Framingham Studies found that for stroke, the risk associated with hypertension falls after 60 reaching no risk by 80.
- A study of over 4000 ambulatory hypertensive patients over 80 found mortality was higher in the 5-year follow-up for those with lower systolic and diastolic blood pressure.
- In a meta-analysis of 61 prospective studies with nearly 12 million person-years follow-up, the risk of death from an obstructive type heart attack (MI) for any given level of cholesterol fell with age, and with participants over 70, total cholesterol was *negatively correlated* with both hemorrhagic and total stroke mortality, particularly with those having systolic blood pressure over about 145 mm Hg.

- In a clinical trial of antihypertensive therapy involving 4000 patient-years, it was found that 98.9% of patients treated experienced no benefit in terms of the endpoint of all strokes, fatal and non-fatal for older individuals. For non-fatal strokes, the number was 99.8% with no benefit.
- In the famous PROSPER study, 6000 older individuals with a history of or risk factor for vascular disease where followed for 3 years. The trial involved a statin vs. a placebo. No statistical significant reduction in stroke was found and for all cardiovascular endpoints, statin therapy failed to benefit 98.3% of the subjects and for the reduction of non-fatal cardiovascular events, 99% saw no benefit.

The author brings up the issue of morbidity associated with statins, providing an estimate of it occurring in 10% (some believe it is 20%) of treated patients, and that there is evidence that these risk are underreported, possibly because of publication bias. This level of prevalence shifts the risk/benefit result to excessive risk.

## COFFEE, YOGURT AND RISK OF DEVELOPING TYPE 2 DIABETES

A systematic review and dose response meta-analysis has just appeared where the issue was drinking coffee and the risk of developing type 2 diabetes.[10] Over one million study participants were involved with follow-ups of 10 months to 20 years. The dose response was remarkable with relative risk reductions based on no or rare consumption as a reference went from 8% for one cup/day to 33% for 6 cups/day. A plot going out 11 years shows a relative risk reduction of about 48%. It was not possible to calculate absolute risk reductions from the data presented. However, the results appear to at least present convincing evidence of no harm. Similar results were obtained for both regular and decaffeinated coffee. The mechanism is not clear. Coffee contains a chemical that reduces glucose absorption in animals and other components may improve glucose metabolism.

Another study also just published examined the impact of consuming dairy products on the incidence of type 2 diabetes.[11] Four thousand subjects, age range 40-79, were followed for eleven years. The only dairy products found to offer significant protection were low-fat fermented dairy products (cheese, sour cream and yogurt). For low-fat yogurt, consuming a mean of 80 g/day (range 44-513g/day) reduced the *absolute* risk of developing type 2 diabetes by almost 7% whereas for low-fat fermented dairy intake, the same mean and range of intake yielded almost a 6% absolute reduction. In studies of this sort, these are large absolute benefits. Models adjusted for various interfering factors provided relative risk reductions of 30-35%, which were statistically significant. Potential mechanisms discussed included increased intake of vitamin K2 and probiotic bacteria improving lipid and antioxidant status, and that these were low energy-density foods which favourably impact fasting insulin levels and the risk of the metabolic syndrome.

Reference List


1. Grandjean P, Landrigan PJ. Neurobehavioural effects of developmental toxicity. *Lancet Neurol.* 2014;13:330-338.
2. Grandjean P. *Only one chance. How environmental pollution impairs brain development*. Oxford University Press; 2013.
3. Rzhetsky A, Bagley SC, Wang K et al. Environmental and state-level regulatory factors affect the incidence of autism and intellectual disability. *PLoS Comput Biol.* 2014;10:e1003518.
4. Mesange R, Defarge J, Seraline G-F. Major pesticides are more toxic to human cells than their declared active principals. *BioMed Res Intl.* 2014;In Press.
5. Tsai TT, Patel UD, Chang TI et al. Contemporary Incidence, Predictors, and Outcomes of Acute Kidney Injury in Patients Undergoing Percutaneous Coronary Interventions: Insights From the NCDR Cath-PCI Registry. *JACC Cardiovasc Interv.* 2014;7:1-9.
6. Chan PS, Patel MR, Klein LW et al. Appropriateness of percutaneous coronary intervention. *JAMA.* 2011;306:53-61.

7. Xu L, Freeman G, Cowling BJ, Schooling CM. Testosterone therapy and cardiovascular events among men: a systematic review and meta-analysis of placebo-controlled randomized trials. *BMC Med.* 2013;11:108.
8. Finkle WD, Greenland S, Ridgeway GK et al. Increased risk of non-fatal myocardial infarction following testosterone therapy prescription in men. *PLoS One.* 2014;9:e85805.
9. Byatt K. Overenthusiastic stroke risk factor modification in the over-80s: Are we being disingenuous to ourselves, and to our oldest patients? *Evid Based Med.* 2014.
10. Ding M, Bhupathiraju SN, Chen M, van Dam RM, Hu FB. Caffeinated and decaffeinated coffee consumption and risk of type 2 diabetes: a systematic review and a dose-response meta-analysis. *Diabetes Care.* 2014;37:569-586.
11. O'Connor LM, Lentjes MA, Luben RN, Khaw KT, Wareham NJ, Forouhi NG. Dietary dairy product intake and incident type 2 diabetes: a prospective study using dietary data from a 7-day food diary. *Diabetologia.* 2014.



**Editor: William R. Ware, PhD**

INTERNATIONAL HEALTH NEWS is published 10 times a year by
Hans R. Larsen MSc ChE, 1320 Point Street, Victoria, BC, Canada, V8S 1A5
E-mail: editor@yourhealthbase.com World Wide Web: http://www.yourhealthbase.com

ISSN 1203-1933 